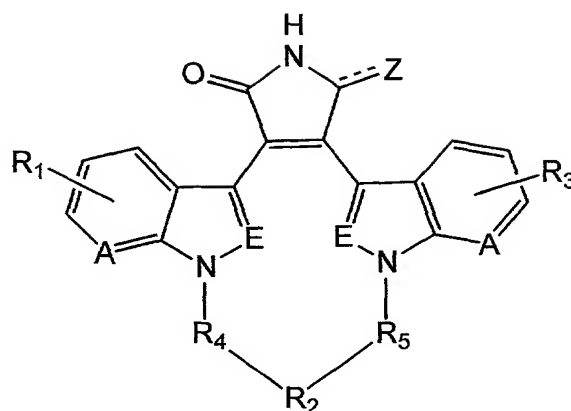


What is Claimed is:

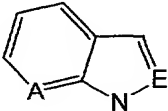
1. A compound of Formula (I):



Formula (I)

wherein

A and E are independently selected from the group consisting of a hydrogen substituted

- 5 carbon atom and a nitrogen atom; wherein  is independently selected from the group consisting of 1*H*-indole, 1*H*-pyrrolo[2,3-*b*]pyridine, 1*H*-pyrazolo[3,4-*b*]pyridine and 1*H*-indazole;

Z is selected from O or dihydro; wherein when Z is dihydro, each hydrogen atom is attached by a single bond;

- 10 R<sub>4</sub> and R<sub>5</sub> are independently selected from C<sub>1-8</sub>alkyl, C<sub>2-8</sub>alkenyl and C<sub>2-8</sub>alkynyl, wherein R<sub>4</sub> and R<sub>5</sub> are optionally substituted with oxo;

- R<sub>2</sub> is selected from the group consisting of -C<sub>1-8</sub>alkyl-, -C<sub>2-8</sub>alkenyl-, -C<sub>2-8</sub>alkynyl-, -O-(C<sub>1-8</sub>)alkyl-O-, -O-(C<sub>2-8</sub>)alkenyl-O-, -O-(C<sub>2-8</sub>)alkynyl-O-, -C(O)-(C<sub>1-8</sub>)alkyl-C(O)- (wherein any of the foregoing alkyl, alkenyl and alkynyl  
15 linking groups are straight carbon chains optionally substituted with one to four substituents independently selected from the group consisting of C<sub>1-8</sub>alkyl, C<sub>1-8</sub>alkoxy, C<sub>1-8</sub>alkoxy(C<sub>1-8</sub>)alkyl, carboxyl, carboxyl(C<sub>1-8</sub>)alkyl, -C(O)O-(C<sub>1-8</sub>)alkyl, -C<sub>1-8</sub>alkyl-C(O)O-(C<sub>1-8</sub>)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and

C<sub>1-4</sub>alkyl), amino(C<sub>1-8</sub>)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), halogen, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkyl, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkoxy, hydroxy, hydroxy(C<sub>1-8</sub>)alkyl and oxo; and, wherein any of the foregoing alkyl, alkenyl and alkynyl linking groups are optionally substituted with one to two substituents independently selected from the group consisting of heterocyclyl, aryl, heteroaryl, heterocyclyl(C<sub>1-8</sub>)alkyl, aryl(C<sub>1-8</sub>)alkyl, heteroaryl(C<sub>1-8</sub>)alkyl, spirocycloalkyl and spiroheterocyclyl (wherein any of the foregoing cycloalkyl, heterocyclyl, aryl and heteroaryl substituents are optionally substituted with one to four substituents independently selected from the group consisting of C<sub>1-8</sub>alkyl, C<sub>1-8</sub>alkoxy, C<sub>1-8</sub>alkoxy(C<sub>1-8</sub>)alkyl, carboxyl, carboxyl(C<sub>1-8</sub>)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), amino(C<sub>1-8</sub>)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), halogen, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkyl, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkoxy, hydroxy and hydroxy(C<sub>1-8</sub>)alkyl; and, wherein any of the foregoing heterocyclyl substituents are optionally substituted with oxo)), cycloalkyl, heterocyclyl, aryl, heteroaryl (wherein cycloalkyl, heterocyclyl, aryl and heteroaryl are optionally substituted with one to four substituents independently selected from the group consisting of C<sub>1-8</sub>alkyl, C<sub>1-8</sub>alkoxy, C<sub>1-8</sub>alkoxy(C<sub>1-8</sub>)alkyl, carboxyl, carboxyl(C<sub>1-8</sub>)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), amino(C<sub>1-8</sub>)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), halogen, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkyl, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkoxy, hydroxy and hydroxy(C<sub>1-8</sub>)alkyl; and, wherein heterocyclyl is optionally substituted with oxo), -(O-(CH<sub>2</sub>)<sub>1-6</sub>)<sub>0-5</sub>-O-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-O-(CH<sub>2</sub>)<sub>1-6</sub>-O-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-O-(CH<sub>2</sub>)<sub>1-6</sub>-O-(CH<sub>2</sub>)<sub>1-6</sub>-O-, -(O-(CH<sub>2</sub>)<sub>1-6</sub>)<sub>0-5</sub>-NR<sub>6</sub>-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-O-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-O-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>6</sub>-, -(O-(CH<sub>2</sub>)<sub>1-6</sub>)<sub>0-5</sub>-S-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-S-(CH<sub>2</sub>)<sub>1-6</sub>-O-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-O-(CH<sub>2</sub>)<sub>1-6</sub>-S-, -NR<sub>6</sub>-, -NR<sub>6</sub>-NR<sub>7</sub>-, -NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>7</sub>-, -NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>7</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>8</sub>-, -NR<sub>6</sub>-C(O)-, -C(O)-NR<sub>6</sub>-, -C(O)-(CH<sub>2</sub>)<sub>0-6</sub>-NR<sub>6</sub>-(CH<sub>2</sub>)<sub>0-6</sub>-C(O)-, -NR<sub>6</sub>-(CH<sub>2</sub>)<sub>0-6</sub>-C(O)-(CH<sub>2</sub>)<sub>1-6</sub>-C(O)-(CH<sub>2</sub>)<sub>0-6</sub>-NR<sub>7</sub>-, -NR<sub>6</sub>-C(O)-NR<sub>7</sub>-, -NR<sub>6</sub>-C(NR<sub>7</sub>)-NR<sub>8</sub>-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-S-, -S-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-O-, -S-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-S-, -NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-S-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>7</sub>- and -SO<sub>2</sub>- (wherein

R<sub>6</sub>, R<sub>7</sub> and R<sub>8</sub> are independently selected from the group consisting of hydrogen, C<sub>1-8</sub>alkyl, C<sub>1-8</sub>alkoxy(C<sub>1-8</sub>)alkyl, carboxyl(C<sub>1-8</sub>)alkyl, amino(C<sub>1-8</sub>)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), hydroxy(C<sub>1-8</sub>)alkyl, heterocyclyl(C<sub>1-8</sub>)alkyl, aryl(C<sub>1-8</sub>)alkyl and heteroaryl(C<sub>1-8</sub>)alkyl (wherein the foregoing heterocyclyl, aryl and heteroaryl substituents are optionally substituted with one to four substituents independently selected from the group consisting of C<sub>1-8</sub>alkyl, C<sub>1-8</sub>alkoxy, C<sub>1-8</sub>alkoxy(C<sub>1-8</sub>)alkyl, carboxyl, carboxyl(C<sub>1-8</sub>)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), amino(C<sub>1-8</sub>)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), halogen, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkyl, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkoxy, hydroxy and hydroxy(C<sub>1-8</sub>)alkyl; and, wherein heterocyclyl is optionally substituted with oxo));

with the proviso that, if A and E are selected from a hydrogen substituted carbon atom, then R<sub>2</sub> is selected from the group consisting of -C<sub>2-8</sub>alkynyl-, -O-(C<sub>1-8</sub>)alkyl-O-, -O-(C<sub>2-8</sub>)alkenyl-O-, -O-(C<sub>2-8</sub>)alkynyl-O-, -C(O)-(C<sub>1-8</sub>)alkyl-C(O)- (wherein any of the foregoing alkyl, alkenyl and alkynyl linking groups are straight carbon chains optionally substituted with one to four substituents independently selected from the group consisting of C<sub>1-8</sub>alkyl, C<sub>1-8</sub>alkoxy, C<sub>1-8</sub>alkoxy(C<sub>1-8</sub>)alkyl, carboxyl, carboxyl(C<sub>1-8</sub>)alkyl, -C(O)O-(C<sub>1-8</sub>)alkyl, -C<sub>1-8</sub>alkyl-C(O)O-(C<sub>1-8</sub>)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), amino(C<sub>1-8</sub>)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), halogen, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkyl, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkoxy, hydroxy, hydroxy(C<sub>1-8</sub>)alkyl and oxo; and, wherein any of the foregoing alkyl, alkenyl and alkynyl linking groups are optionally substituted with one to two substituents independently selected from the group consisting of heterocyclyl, aryl, heteroaryl, heterocyclyl(C<sub>1-8</sub>)alkyl, aryl(C<sub>1-8</sub>)alkyl, heteroaryl(C<sub>1-8</sub>)alkyl, spirocycloalkyl and spiroheterocyclyl (wherein any of the foregoing cycloalkyl, heterocyclyl, aryl and heteroaryl substituents are optionally substituted with one to four substituents independently selected from the group consisting of C<sub>1-8</sub>alkyl, C<sub>1-8</sub>alkoxy, C<sub>1-8</sub>alkoxy(C<sub>1-8</sub>)alkyl, carboxyl, carboxyl(C<sub>1-8</sub>)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and

C<sub>1-4</sub>alkyl), amino(C<sub>1-8</sub>)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), halogen, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkyl, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkoxy, hydroxy and hydroxy(C<sub>1-8</sub>)alkyl; and, wherein any of the foregoing heterocyclyl substituents are optionally substituted with oxo)), cycloalkyl (wherein cycloalkyl is optionally substituted with one to four substituents independently selected from the group consisting of C<sub>1-8</sub>alkyl, C<sub>1-8</sub>alkoxy, C<sub>1-8</sub>alkoxy(C<sub>1-8</sub>)alkyl, carboxyl, carboxyl(C<sub>1-8</sub>)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), amino(C<sub>1-8</sub>)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), halogen, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkyl, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkoxy, hydroxy and hydroxy(C<sub>1-8</sub>)alkyl), -(O-(CH<sub>2</sub>)<sub>1-6</sub>)<sub>1-5</sub>-O-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-O-(CH<sub>2</sub>)<sub>1-6</sub>-O-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-O-(CH<sub>2</sub>)<sub>1-6</sub>-O-(CH<sub>2</sub>)<sub>1-6</sub>-O-, -(O-(CH<sub>2</sub>)<sub>1-6</sub>)<sub>1-5</sub>-NR<sub>6</sub>-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-O-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-O-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>6</sub>-, -(O-(CH<sub>2</sub>)<sub>1-6</sub>)<sub>0-5</sub>-S-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-S-(CH<sub>2</sub>)<sub>1-6</sub>-O-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-O-(CH<sub>2</sub>)<sub>1-6</sub>-S-, -NR<sub>6</sub>-NR<sub>7</sub>-, -NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>7</sub>-, -NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>7</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>8</sub>-, -NR<sub>9</sub>-C(O)-, -C(O)-NR<sub>9</sub>-, -C(O)-(CH<sub>2</sub>)<sub>0-6</sub>-NR<sub>6</sub>-(CH<sub>2</sub>)<sub>0-6</sub>-C(O)-, -NR<sub>6</sub>-(CH<sub>2</sub>)<sub>0-6</sub>-C(O)-(CH<sub>2</sub>)<sub>1-6</sub>-C(O)-(CH<sub>2</sub>)<sub>0-6</sub>-NR<sub>7</sub>-, -NR<sub>6</sub>-C(O)-NR<sub>7</sub>-, -NR<sub>6</sub>-C(NR<sub>7</sub>)-NR<sub>8</sub>-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-S-, -S-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-O-, -S-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-S- and -NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-S-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>7</sub>- (wherein R<sub>6</sub>, R<sub>7</sub> and R<sub>8</sub> are independently selected from the group consisting of hydrogen, C<sub>1-8</sub>alkyl, C<sub>1-8</sub>alkoxy(C<sub>1-8</sub>)alkyl, carboxyl(C<sub>1-8</sub>)alkyl, amino(C<sub>1-8</sub>)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), hydroxy(C<sub>1-8</sub>)alkyl, heterocyclyl(C<sub>1-8</sub>)alkyl, aryl(C<sub>1-8</sub>)alkyl and heteroaryl(C<sub>1-8</sub>)alkyl (wherein the foregoing heterocyclyl, aryl and heteroaryl substituents are optionally substituted with one to four substituents independently selected from the group consisting of C<sub>1-8</sub>alkyl, C<sub>1-8</sub>alkoxy, C<sub>1-8</sub>alkoxy(C<sub>1-8</sub>)alkyl, carboxyl, carboxyl(C<sub>1-8</sub>)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), amino(C<sub>1-8</sub>)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), halogen, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkyl, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkoxy, hydroxy and hydroxy(C<sub>1-8</sub>)alkyl; and, wherein heterocyclyl is optionally substituted with oxo); and, wherein R<sub>9</sub> is selected from the group

consisting of C<sub>1-8</sub>alkyl, C<sub>1-8</sub>alkoxy(C<sub>1-8</sub>)alkyl, carboxyl(C<sub>1-8</sub>)alkyl, amino(C<sub>1-8</sub>)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), hydroxy(C<sub>1-8</sub>)alkyl, heterocyclyl(C<sub>1-8</sub>)alkyl, aryl(C<sub>1-8</sub>)alkyl and heteroaryl(C<sub>1-8</sub>)alkyl (wherein the foregoing heterocyclyl, aryl and heteroaryl substituents are optionally substituted with one to four substituents independently selected from the group consisting of C<sub>1-8</sub>alkyl, C<sub>1-8</sub>alkoxy, C<sub>1-8</sub>alkoxy(C<sub>1-8</sub>)alkyl, carboxyl, carboxyl(C<sub>1-8</sub>)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), amino(C<sub>1-8</sub>)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), halogen, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkyl, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkoxy, hydroxy and hydroxy(C<sub>1-8</sub>)alkyl; and, wherein heterocyclyl is optionally substituted with oxo)); and,

R<sub>1</sub> and R<sub>3</sub> are independently selected from the group consisting of hydrogen, C<sub>1-8</sub>alkyl, C<sub>2-8</sub>alkenyl, C<sub>2-8</sub>alkynyl (wherein alkyl, alkenyl and alkynyl are optionally substituted with a substituent selected from the group consisting of C<sub>1-8</sub>alkoxy, alkoxy(C<sub>1-8</sub>)alkyl, carboxyl, carboxyl(C<sub>1-8</sub>)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), amino(C<sub>1-8</sub>)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), (halo)<sub>1-3</sub>, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkyl, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkoxy, hydroxy, hydroxy(C<sub>1-8</sub>)alkyl and oxo), C<sub>1-8</sub>alkoxy, C<sub>1-8</sub>alkoxycarbonyl, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkoxy, C<sub>1-8</sub>alkylthio, aryl, heteroaryl (wherein aryl and heteroaryl are optionally substituted with a substituent selected from the group consisting of C<sub>1-8</sub>alkyl, C<sub>1-8</sub>alkoxy, alkoxy(C<sub>1-8</sub>)alkyl, carboxyl, carboxyl(C<sub>1-8</sub>)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), amino(C<sub>1-8</sub>)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), halogen, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkyl, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkoxy, hydroxy and hydroxy(C<sub>1-8</sub>)alkyl), amino (substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), cyano, halogen, hydroxy and nitro;

and pharmaceutically acceptable salts thereof.

2. The compound of claim 1 wherein R<sub>4</sub> and R<sub>5</sub> are independently selected from C<sub>1-6</sub>alkyl, C<sub>2-6</sub>alkenyl and C<sub>2-6</sub>alkynyl optionally substituted with oxo.
3. The compound of claim 1 wherein R<sub>4</sub> and R<sub>5</sub> are independently selected from C<sub>1-6</sub>alkyl, C<sub>2-6</sub>alkenyl and C<sub>2-6</sub>alkynyl.
4. The compound of claim 1 wherein R<sub>4</sub> and R<sub>5</sub> are independently selected from C<sub>1-6</sub>alkyl.
5. The compound of claim 1 wherein R<sub>2</sub> is selected from the group consisting of -C<sub>1-8</sub>alkyl-, -C<sub>2-4</sub>alkenyl-, -C<sub>2-4</sub>alkynyl-, -O-(C<sub>1-4</sub>)alkyl-O-, -O-(C<sub>2-4</sub>)alkenyl-O-, -O-(C<sub>2-4</sub>)alkynyl-O-, -C(O)-(C<sub>1-4</sub>)alkyl-C(O)- (wherein any of the foregoing alkyl, alkenyl and alkynyl linking groups are straight carbon chains optionally substituted with one to four substituents independently selected from the group consisting of C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy, C<sub>1-4</sub>alkoxy(C<sub>1-4</sub>)alkyl, carboxyl, carboxyl(C<sub>1-4</sub>)alkyl, -C(O)O-(C<sub>1-4</sub>)alkyl, -C<sub>1-4</sub>alkyl-C(O)O-(C<sub>1-4</sub>)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), amino(C<sub>1-4</sub>)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), halogen, (halo)<sub>1-3</sub>(C<sub>1-4</sub>)alkyl, (halo)<sub>1-3</sub>(C<sub>1-4</sub>)alkoxy, hydroxy, hydroxy(C<sub>1-4</sub>)alkyl and oxo; and, wherein any of the foregoing alkyl, alkenyl and alkynyl linking groups are optionally substituted with one to two substituents independently selected from the group consisting of heterocyclyl, aryl, heteroaryl, heterocyclyl(C<sub>1-4</sub>)alkyl, aryl(C<sub>1-4</sub>)alkyl, heteroaryl(C<sub>1-4</sub>)alkyl, spirocycloalkyl and spiroheterocyclyl (wherein any of the foregoing cycloalkyl, heterocyclyl, aryl and heteroaryl substituents are optionally substituted with one to four substituents independently selected from the group consisting of C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy, C<sub>1-4</sub>alkoxy(C<sub>1-4</sub>)alkyl, carboxyl, carboxyl(C<sub>1-4</sub>)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), amino(C<sub>1-4</sub>)alkyl (wherein amino is

substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), halogen, (halo)<sub>1-3</sub>(C<sub>1-4</sub>)alkyl, (halo)<sub>1-3</sub>(C<sub>1-4</sub>)alkoxy, hydroxy and hydroxy(C<sub>1-4</sub>)alkyl; and, wherein any of the foregoing heterocyclyl substituents are optionally substituted with oxo)), cycloalkyl, heterocyclyl, aryl, heteroaryl (wherein cycloalkyl, heterocyclyl, aryl and heteroaryl are optionally substituted with one to four substituents independently selected from the group consisting of C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy, C<sub>1-4</sub>alkoxy(C<sub>1-4</sub>)alkyl, carboxyl, carboxyl(C<sub>1-4</sub>)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), amino(C<sub>1-4</sub>)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), halogen, (halo)<sub>1-3</sub>(C<sub>1-4</sub>)alkyl, (halo)<sub>1-3</sub>(C<sub>1-4</sub>)alkoxy, hydroxy and hydroxy(C<sub>1-4</sub>)alkyl; and, wherein heterocyclyl is optionally substituted with oxo), -(O-(CH<sub>2</sub>)<sub>1-6</sub>)<sub>0-5</sub>-O-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-O-(CH<sub>2</sub>)<sub>1-6</sub>-O-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-O-(CH<sub>2</sub>)<sub>1-6</sub>-O-(CH<sub>2</sub>)<sub>1-6</sub>-O-, -(O-(CH<sub>2</sub>)<sub>1-6</sub>)<sub>0-5</sub>-NR<sub>6</sub>-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-O-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-O-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>6</sub>-, -(O-(CH<sub>2</sub>)<sub>1-6</sub>)<sub>0-5</sub>-S-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-S-(CH<sub>2</sub>)<sub>1-6</sub>-O-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-O-(CH<sub>2</sub>)<sub>1-6</sub>-S-, -NR<sub>6</sub>-, -NR<sub>6</sub>-NR<sub>7</sub>-, -NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>7</sub>-, -NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>7</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>8</sub>-, -NR<sub>6</sub>-C(O)-, -C(O)-NR<sub>6</sub>-, -C(O)-(CH<sub>2</sub>)<sub>0-6</sub>-NR<sub>6</sub>-(CH<sub>2</sub>)<sub>0-6</sub>-C(O)-, -NR<sub>6</sub>-(CH<sub>2</sub>)<sub>0-6</sub>-C(O)-(CH<sub>2</sub>)<sub>1-6</sub>-C(O)-(CH<sub>2</sub>)<sub>0-6</sub>-NR<sub>7</sub>-, -NR<sub>6</sub>-C(O)-NR<sub>7</sub>-, -NR<sub>6</sub>-C(NR<sub>7</sub>)-NR<sub>8</sub>-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-S-, -S-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-O-, -S-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-S-, -NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-S-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>7</sub>- and -SO<sub>2</sub>- (wherein R<sub>6</sub>, R<sub>7</sub> and R<sub>8</sub> are independently selected from the group consisting of hydrogen, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy(C<sub>1-4</sub>)alkyl, carboxyl(C<sub>1-4</sub>)alkyl, amino(C<sub>1-4</sub>)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), hydroxy(C<sub>1-4</sub>)alkyl, heterocyclyl(C<sub>1-4</sub>)alkyl, aryl(C<sub>1-4</sub>)alkyl and heteroaryl(C<sub>1-4</sub>)alkyl (wherein the foregoing heterocyclyl, aryl and heteroaryl substituents are optionally substituted with one to four substituents independently selected from the group consisting of C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy, C<sub>1-4</sub>alkoxy(C<sub>1-4</sub>)alkyl, carboxyl, carboxyl(C<sub>1-4</sub>)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), amino(C<sub>1-4</sub>)alkyl (wherein amino is substituted with a substituent

with the proviso that, if A and E are selected from a hydrogen substituted carbon atom, then R<sub>2</sub> is selected from the group consisting of -C<sub>2-4</sub>alkynyl-, -O-(C<sub>1-4</sub>)alkyl-O-, -O-(C<sub>2-4</sub>)alkenyl-O-, -O-(C<sub>2-4</sub>)alkynyl-O-, -C(O)-(C<sub>1-4</sub>)alkyl-C(O)- (wherein any of the foregoing alkyl, alkenyl and alkynyl linking groups are straight carbon chains optionally substituted with one to four substituents independently selected from the group consisting of C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy, C<sub>1-4</sub>alkoxy(C<sub>1-4</sub>)alkyl, carboxyl, carboxyl(C<sub>1-4</sub>)alkyl, -C(O)O-(C<sub>1-4</sub>)alkyl, -C<sub>1-4</sub>alkyl-C(O)O-(C<sub>1-4</sub>)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), amino(C<sub>1-4</sub>)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), halogen, (halo)<sub>1-3</sub>(C<sub>1-4</sub>)alkyl, (halo)<sub>1-3</sub>(C<sub>1-4</sub>)alkoxy, hydroxy, hydroxy(C<sub>1-4</sub>)alkyl and oxo; and, wherein any of the foregoing alkyl, alkenyl and alkynyl linking groups are optionally substituted with one to two substituents independently selected from the group consisting of heterocyclyl, aryl, heteroaryl, heterocyclyl(C<sub>1-4</sub>)alkyl, aryl(C<sub>1-4</sub>)alkyl, heteroaryl(C<sub>1-4</sub>)alkyl, spirocycloalkyl and spiroheterocyclyl (wherein any of the foregoing cycloalkyl, heterocyclyl, aryl and heteroaryl substituents are optionally substituted with one to four substituents independently selected from the group consisting of C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy, C<sub>1-4</sub>alkoxy(C<sub>1-4</sub>)alkyl, carboxyl, carboxyl(C<sub>1-4</sub>)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), amino(C<sub>1-4</sub>)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), halogen, (halo)<sub>1-3</sub>(C<sub>1-4</sub>)alkyl, (halo)<sub>1-3</sub>(C<sub>1-4</sub>)alkoxy, hydroxy and hydroxy(C<sub>1-4</sub>)alkyl; and, wherein any of the foregoing heterocyclyl substituents are optionally substituted with oxo)), cycloalkyl (wherein cycloalkyl is optionally substituted with one to four substituents independently selected from the group consisting of C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy, C<sub>1-4</sub>alkoxy(C<sub>1-4</sub>)alkyl, carboxyl, carboxyl(C<sub>1-4</sub>)alkyl, amino (substituted with a substituent independently



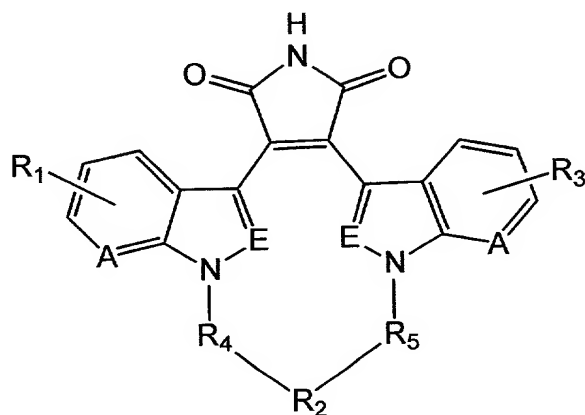
selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), amino(C<sub>1-4</sub>)alkyl  
 (wherein amino is substituted with a substituent independently selected from the  
 group consisting of hydrogen and C<sub>1-4</sub>alkyl), halogen, (halo)<sub>1-3</sub>(C<sub>1-4</sub>)alkyl,  
 (halo)<sub>1-3</sub>(C<sub>1-4</sub>)alkoxy, hydroxy and hydroxy(C<sub>1-4</sub>)alkyl), -(O-(CH<sub>2</sub>)<sub>1-6</sub>)<sub>1-5</sub>-O-,  
 5 -O-(CH<sub>2</sub>)<sub>1-6</sub>-O-(CH<sub>2</sub>)<sub>1-6</sub>-O-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-O-(CH<sub>2</sub>)<sub>1-6</sub>-O-(CH<sub>2</sub>)<sub>1-6</sub>-O-,  
 -(O-(CH<sub>2</sub>)<sub>1-6</sub>)<sub>1-5</sub>-NR<sub>6</sub>-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-O-,  
 -O-(CH<sub>2</sub>)<sub>1-6</sub>-O-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>6</sub>-, -(O-(CH<sub>2</sub>)<sub>1-6</sub>)<sub>0-5</sub>-S-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-S-(CH<sub>2</sub>)<sub>1-6</sub>-O-,  
 -O-(CH<sub>2</sub>)<sub>1-6</sub>-O-(CH<sub>2</sub>)<sub>1-6</sub>-S-, -NR<sub>6</sub>-NR<sub>7</sub>-, -NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>7</sub>-,  
 -NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>7</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>8</sub>-, -NR<sub>9</sub>-C(O)-, -C(O)-NR<sub>9</sub>-,  
 10 -C(O)-(CH<sub>2</sub>)<sub>0-6</sub>-NR<sub>6</sub>-(CH<sub>2</sub>)<sub>0-6</sub>-C(O)-,  
 -NR<sub>6</sub>-(CH<sub>2</sub>)<sub>0-6</sub>-C(O)-(CH<sub>2</sub>)<sub>1-6</sub>-C(O)-(CH<sub>2</sub>)<sub>0-6</sub>-NR<sub>7</sub>-, -NR<sub>6</sub>-C(O)-NR<sub>7</sub>-,  
 -NR<sub>6</sub>-C(NR<sub>7</sub>)-NR<sub>8</sub>-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-S-, -S-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-O-,  
 -S-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-S- and -NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-S-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>7</sub>- (wherein R<sub>6</sub>,  
 R<sub>7</sub> and R<sub>8</sub> are independently selected from the group consisting of hydrogen,  
 15 C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy(C<sub>1-4</sub>)alkyl, carboxyl(C<sub>1-4</sub>)alkyl, amino(C<sub>1-4</sub>)alkyl (wherein  
 amino is substituted with a substituent independently selected from the group  
 consisting of hydrogen and C<sub>1-4</sub>alkyl), hydroxy(C<sub>1-4</sub>)alkyl,  
 heterocyclyl(C<sub>1-4</sub>)alkyl, aryl(C<sub>1-4</sub>)alkyl and heteroaryl(C<sub>1-4</sub>)alkyl (wherein the  
 foregoing heterocyclyl, aryl and heteroaryl substituents are optionally  
 20 substituted with one to four substituents independently selected from the group  
 consisting of C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy, C<sub>1-4</sub>alkoxy(C<sub>1-4</sub>)alkyl, carboxyl,  
 carboxyl(C<sub>1-4</sub>)alkyl, amino (substituted with a substituent independently  
 selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), amino(C<sub>1-4</sub>)alkyl  
 (wherein amino is substituted with a substituent independently selected from the  
 25 group consisting of hydrogen and C<sub>1-4</sub>alkyl), halogen, (halo)<sub>1-3</sub>(C<sub>1-4</sub>)alkyl,  
 (halo)<sub>1-3</sub>(C<sub>1-4</sub>)alkoxy, hydroxy and hydroxy(C<sub>1-4</sub>)alkyl; and, wherein  
 heterocyclyl is optionally substituted with oxo); and, wherein R<sub>9</sub> is selected  
 from the group consisting of C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy(C<sub>1-4</sub>)alkyl,  
 carboxyl(C<sub>1-4</sub>)alkyl, amino(C<sub>1-4</sub>)alkyl (wherein amino is substituted with a  
 30 substituent independently selected from the group consisting of hydrogen and  
 C<sub>1-4</sub>alkyl), hydroxy(C<sub>1-4</sub>)alkyl, heterocyclyl(C<sub>1-4</sub>)alkyl, aryl(C<sub>1-4</sub>)alkyl and  
 heteroaryl(C<sub>1-4</sub>)alkyl (wherein the foregoing heterocyclyl, aryl and heteroaryl  
 substituents are optionally substituted with one to four substituents

- independently selected from the group consisting of C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy, C<sub>1-4</sub>alkoxy(C<sub>1-4</sub>)alkyl, carboxyl, carboxyl(C<sub>1-4</sub>)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), amino(C<sub>1-4</sub>)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), halogen, (halo)<sub>1-3</sub>(C<sub>1-4</sub>)alkyl, (halo)<sub>1-3</sub>(C<sub>1-4</sub>)alkoxy, hydroxy and hydroxy(C<sub>1-4</sub>)alkyl; and, wherein heterocyclyl is optionally substituted with oxo)).
- 5
6. The compound of claim 1 wherein R<sub>2</sub> is selected from the group consisting of
- 10 -C<sub>1-8</sub>alkyl- (optionally substituted with one to three substituents independently selected from the group consisting of halogen, hydroxy and oxo); aryl, heteroaryl, -(O-(CH<sub>2</sub>)<sub>1-6</sub>)<sub>0-5</sub>-O-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-O-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-S-(CH<sub>2</sub>)<sub>1-6</sub>-O- and -NR<sub>6</sub>- (wherein R<sub>6</sub>, R<sub>7</sub> and R<sub>8</sub> are independently selected from the group consisting of hydrogen, C<sub>1-4</sub>alkyl and
- 15 C<sub>1-4</sub>alkoxy(C<sub>1-4</sub>)alkyl);
- with the proviso that, if A and E are selected from a hydrogen substituted carbon atom, then R<sub>2</sub> is selected from the group consisting of
- (O-(CH<sub>2</sub>)<sub>1-6</sub>)<sub>1-5</sub>-O-, -(O-(CH<sub>2</sub>)<sub>1-6</sub>)<sub>1-5</sub>-NR<sub>6</sub>-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-O- and -NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>7</sub> - (CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>8</sub>- (wherein R<sub>6</sub>, R<sub>7</sub> and R<sub>8</sub> are independently
- 20 selected from the group consisting of hydrogen, C<sub>1-4</sub>alkyl and hydroxy(C<sub>1-4</sub>)alkyl).
7. The compound of claim 1 wherein R<sub>2</sub> is selected from the group consisting of
- C<sub>1-8</sub>alkyl- (optionally substituted with one to two substituents independently selected from the group consisting of halogen, hydroxy and oxo); phenyl,
- 25 pyridinyl, -(O-(CH<sub>2</sub>)<sub>2</sub>)<sub>1-4</sub>-O-, -O-(CH<sub>2</sub>)<sub>2</sub>-NR<sub>6</sub>-(CH<sub>2</sub>)<sub>2</sub>-O-, -O-(CH<sub>2</sub>)<sub>2</sub>-S-(CH<sub>2</sub>)<sub>2</sub>-O- and -NR<sub>6</sub>- (wherein R<sub>6</sub>, R<sub>7</sub> and R<sub>8</sub> are independently selected from the group consisting of hydrogen, C<sub>1-3</sub>alkyl and C<sub>1-2</sub>alkoxy(C<sub>1-2</sub>)alkyl);
- with the proviso that, if A and E are selected from a hydrogen substituted carbon atom, then R<sub>2</sub> is selected from the group consisting of
- 30 -(O-(CH<sub>2</sub>)<sub>2</sub>)<sub>1-4</sub>-O-, -(O-(CH<sub>2</sub>)<sub>2</sub>)<sub>2</sub>-NR<sub>6</sub>-, -O-(CH<sub>2</sub>)<sub>2</sub>-NR<sub>6</sub>-(CH<sub>2</sub>)<sub>2</sub>-O- and

-NR<sub>6</sub>-(CH<sub>2</sub>)<sub>2</sub>-NR<sub>7</sub>-(CH<sub>2</sub>)<sub>2</sub>-NR<sub>8</sub>- (wherein R<sub>6</sub>, R<sub>7</sub> and R<sub>8</sub> are independently selected from the group consisting of hydrogen, C<sub>1-3</sub>alkyl and hydroxy(C<sub>1-2</sub>)alkyl).

8. The compound of claim 1 wherein R<sub>1</sub> and R<sub>3</sub> are independently selected from the group consisting of hydrogen, C<sub>1-4</sub>alkyl, C<sub>2-4</sub>alkenyl, C<sub>2-4</sub>alkynyl (wherein alkyl, alkenyl and alkynyl are optionally substituted with a substituent selected from the group consisting of C<sub>1-4</sub>alkoxy, alkoxy(C<sub>1-4</sub>)alkyl, carboxyl, carboxyl(C<sub>1-4</sub>)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), amino(C<sub>1-4</sub>)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), (halo)<sub>1-3</sub>, (halo)<sub>1-3</sub>(C<sub>1-4</sub>)alkyl, (halo)<sub>1-3</sub>(C<sub>1-4</sub>)alkoxy, hydroxy, hydroxy(C<sub>1-4</sub>)alkyl and oxo), C<sub>1-4</sub>alkoxy, C<sub>1-4</sub>alkoxycarbonyl, (halo)<sub>1-3</sub>(C<sub>1-4</sub>)alkoxy, C<sub>1-4</sub>alkylthio, aryl, heteroaryl (wherein aryl and heteroaryl are optionally substituted with a substituent selected from the group consisting of C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy, alkoxy(C<sub>1-4</sub>)alkyl, carboxyl, carboxyl(C<sub>1-4</sub>)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), amino(C<sub>1-4</sub>)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), halogen, (halo)<sub>1-3</sub>(C<sub>1-4</sub>)alkyl, (halo)<sub>1-3</sub>(C<sub>1-4</sub>)alkoxy, hydroxy and hydroxy(C<sub>1-4</sub>)alkyl), amino (substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), cyano, halogen, hydroxy and nitro.
9. The compound of claim 1 wherein R<sub>1</sub> and R<sub>3</sub> are independently selected from the group consisting of hydrogen, C<sub>1-4</sub>alkyl (optionally substituted with a substituent selected from the group consisting of C<sub>1-4</sub>alkoxy, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), (halo)<sub>1-3</sub>, hydroxy and oxo), C<sub>1-4</sub>alkoxy, C<sub>1-4</sub>alkoxycarbonyl, (halo)<sub>1-3</sub>(C<sub>1-4</sub>)alkoxy, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), halogen, hydroxy and nitro.

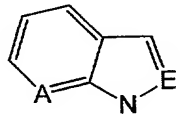
10. The compound of claim 1 wherein  $R_1$  and  $R_3$  are hydrogen.
11. The compound of claim 1 wherein a compound of Formula (I) is selected from a compound of Formula (Iaa):



Formula (Iaa)

wherein

- 5 A and E are independently selected from the group consisting of a hydrogen substituted

carbon atom and a nitrogen atom; wherein  is independently selected from the group consisting of 1H-indole, 1H-pyrrolo[2,3-b]pyridine and 1H-indazole;

- $R_4$  and  $R_5$  are independently selected from  $C_{1-8}$ alkyl,  $C_{2-8}$ alkenyl and  $C_{2-8}$ alkynyl  
10 optionally substituted with oxo;

- $R_2$  is selected from the group consisting of  $-C_{1-8}$ alkyl-,  $-C_{2-8}$ alkenyl-,  $-C_{2-8}$ alkynyl-,  
-O-( $C_{1-8}$ )alkyl-O-, -O-( $C_{2-8}$ )alkenyl-O-, -O-( $C_{2-8}$ )alkynyl-O-,  
-C(O)-( $C_{1-8}$ )alkyl-C(O)- (wherein any of the foregoing alkyl, alkenyl and alkynyl  
15 linking groups are straight carbon chains optionally substituted with one to four  
substituents independently selected from the group consisting of  $C_{1-8}$ alkyl,  
 $C_{1-8}$ alkoxy,  $C_{1-8}$ alkoxy( $C_{1-8}$ )alkyl, carboxyl, carboxyl( $C_{1-8}$ )alkyl,  
-C(O)O-( $C_{1-8}$ )alkyl, - $C_{1-8}$ alkyl-C(O)O-( $C_{1-8}$ )alkyl, amino (substituted with a  
substituent independently selected from the group consisting of hydrogen and

C<sub>1-4</sub>alkyl), amino(C<sub>1-8</sub>)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), halogen, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkyl, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkoxy, hydroxy, hydroxy(C<sub>1-8</sub>)alkyl and oxo; and, wherein any of the foregoing alkyl, alkenyl and alkynyl linking groups are optionally substituted with one to two substituents independently selected from the group consisting of heterocyclyl, aryl, heteroaryl, heterocyclyl(C<sub>1-8</sub>)alkyl, aryl(C<sub>1-8</sub>)alkyl, heteroaryl(C<sub>1-8</sub>)alkyl, spirocycloalkyl and spiroheterocyclyl (wherein any of the foregoing cycloalkyl, heterocyclyl, aryl and heteroaryl substituents are optionally substituted with one to four substituents independently selected from the group consisting of C<sub>1-8</sub>alkyl, C<sub>1-8</sub>alkoxy, C<sub>1-8</sub>alkoxy(C<sub>1-8</sub>)alkyl, carboxyl, carboxyl(C<sub>1-8</sub>)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), amino(C<sub>1-8</sub>)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), halogen, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkyl, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkoxy, hydroxy and hydroxy(C<sub>1-8</sub>)alkyl; and, wherein any of the foregoing heterocyclyl substituents are optionally substituted with oxo)), cycloalkyl, heterocyclyl, aryl, heteroaryl (wherein cycloalkyl, heterocyclyl, aryl and heteroaryl are optionally substituted with one to four substituents independently selected from the group consisting of C<sub>1-8</sub>alkyl, C<sub>1-8</sub>alkoxy, C<sub>1-8</sub>alkoxy(C<sub>1-8</sub>)alkyl, carboxyl, carboxyl(C<sub>1-8</sub>)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), amino(C<sub>1-8</sub>)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), halogen, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkyl, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkoxy, hydroxy and hydroxy(C<sub>1-8</sub>)alkyl; and, wherein heterocyclyl is optionally substituted with oxo), -(O-(CH<sub>2</sub>)<sub>1-6</sub>)<sub>0-5</sub>-O-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-O-(CH<sub>2</sub>)<sub>1-6</sub>-O-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-O-(CH<sub>2</sub>)<sub>1-6</sub>-O-(CH<sub>2</sub>)<sub>1-6</sub>-O-, -(O-(CH<sub>2</sub>)<sub>1-6</sub>)<sub>0-5</sub>-NR<sub>6</sub>-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-O-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-O-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>6</sub>-, -(O-(CH<sub>2</sub>)<sub>1-6</sub>)<sub>0-5</sub>-S-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-S-(CH<sub>2</sub>)<sub>1-6</sub>-O-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-O-(CH<sub>2</sub>)<sub>1-6</sub>-S-, -NR<sub>6</sub>-, -NR<sub>6</sub>-NR<sub>7</sub>-, -NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>7</sub>-, -NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>7</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>8</sub>-, -NR<sub>6</sub>-C(O)-, -C(O)-NR<sub>6</sub>-, -C(O)-(CH<sub>2</sub>)<sub>0-6</sub>-NR<sub>6</sub>-(CH<sub>2</sub>)<sub>0-6</sub>-C(O)-, -NR<sub>6</sub>-(CH<sub>2</sub>)<sub>0-6</sub>-C(O)-(CH<sub>2</sub>)<sub>1-6</sub>-C(O)-(CH<sub>2</sub>)<sub>0-6</sub>-NR<sub>7</sub>-, -NR<sub>6</sub>-C(O)-NR<sub>7</sub>-, -NR<sub>6</sub>-C(NR<sub>7</sub>)-NR<sub>8</sub>-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-S-, -S-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-O-, -S-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-S-, -NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-S-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>7</sub>- and -SO<sub>2</sub>- (wherein

R<sub>6</sub>, R<sub>7</sub> and R<sub>8</sub> are independently selected from the group consisting of hydrogen, C<sub>1-8</sub>alkyl, C<sub>1-8</sub>alkoxy(C<sub>1-8</sub>)alkyl, carboxyl(C<sub>1-8</sub>)alkyl, amino(C<sub>1-8</sub>)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), hydroxy(C<sub>1-8</sub>)alkyl, heterocyclyl(C<sub>1-8</sub>)alkyl, aryl(C<sub>1-8</sub>)alkyl and heteroaryl(C<sub>1-8</sub>)alkyl (wherein the foregoing heterocyclyl, aryl and heteroaryl substituents are optionally substituted with one to four substituents independently selected from the group consisting of C<sub>1-8</sub>alkyl, C<sub>1-8</sub>alkoxy, C<sub>1-8</sub>alkoxy(C<sub>1-8</sub>)alkyl, carboxyl, carboxyl(C<sub>1-8</sub>)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), amino(C<sub>1-8</sub>)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), halogen, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkyl, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkoxy, hydroxy and hydroxy(C<sub>1-8</sub>)alkyl; and, wherein heterocyclyl is optionally substituted with oxo));

with the proviso that, if A and E are selected from a hydrogen substituted carbon atom, then R<sub>2</sub> is selected from the group consisting of -C<sub>2-8</sub>alkynyl-, -O-(C<sub>1-8</sub>)alkyl-O-, -O-(C<sub>2-8</sub>)alkenyl-O-, -O-(C<sub>2-8</sub>)alkynyl-O-, -C(O)-(C<sub>1-8</sub>)alkyl-C(O)- (wherein any of the foregoing alkyl, alkenyl and alkynyl linking groups are straight carbon chains optionally substituted with one to four substituents independently selected from the group consisting of C<sub>1-8</sub>alkyl, C<sub>1-8</sub>alkoxy, C<sub>1-8</sub>alkoxy(C<sub>1-8</sub>)alkyl, carboxyl, carboxyl(C<sub>1-8</sub>)alkyl, -C(O)O-(C<sub>1-8</sub>)alkyl, -C<sub>1-8</sub>alkyl-C(O)O-(C<sub>1-8</sub>)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), amino(C<sub>1-8</sub>)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), halogen, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkyl, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkoxy, hydroxy, hydroxy(C<sub>1-8</sub>)alkyl and oxo; and, wherein any of the foregoing alkyl, alkenyl and alkynyl linking groups are optionally substituted with one to two substituents independently selected from the group consisting of heterocyclyl, aryl, heteroaryl, heterocyclyl(C<sub>1-8</sub>)alkyl, aryl(C<sub>1-8</sub>)alkyl, heteroaryl(C<sub>1-8</sub>)alkyl, spirocycloalkyl and spiroheterocyclyl (wherein any of the foregoing cycloalkyl, heterocyclyl, aryl and heteroaryl substituents are optionally substituted with one to four substituents independently selected from the group consisting of C<sub>1-8</sub>alkyl, C<sub>1-8</sub>alkoxy, C<sub>1-8</sub>alkoxy(C<sub>1-8</sub>)alkyl, carboxyl, carboxyl(C<sub>1-8</sub>)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and

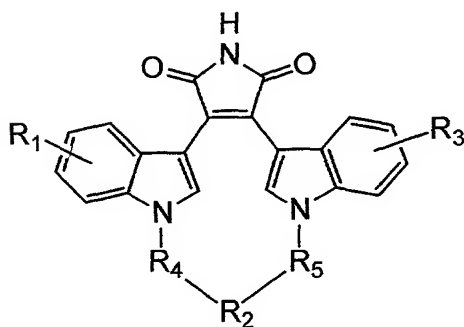
C<sub>1-4</sub>alkyl), amino(C<sub>1-8</sub>)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), halogen, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkyl, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkoxy, hydroxy and hydroxy(C<sub>1-8</sub>)alkyl; and, wherein any of the foregoing heterocyclyl substituents are optionally substituted with oxo)), cycloalkyl (wherein cycloalkyl is optionally substituted with one to four substituents independently selected from the group consisting of C<sub>1-8</sub>alkyl, C<sub>1-8</sub>alkoxy, C<sub>1-8</sub>alkoxy(C<sub>1-8</sub>)alkyl, carboxyl, carboxyl(C<sub>1-8</sub>)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), amino(C<sub>1-8</sub>)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), halogen, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkyl, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkoxy, hydroxy and hydroxy(C<sub>1-8</sub>)alkyl), -(O-(CH<sub>2</sub>)<sub>1-6</sub>)<sub>1-5</sub>-O-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-O-(CH<sub>2</sub>)<sub>1-6</sub>-O-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-O-(CH<sub>2</sub>)<sub>1-6</sub>-O-(CH<sub>2</sub>)<sub>1-6</sub>-O-, -(O-(CH<sub>2</sub>)<sub>1-6</sub>)<sub>1-5</sub>-NR<sub>6</sub>-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-O-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-O-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>6</sub>-, -(O-(CH<sub>2</sub>)<sub>1-6</sub>)<sub>0-5</sub>-S-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-S-(CH<sub>2</sub>)<sub>1-6</sub>-O-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-O-(CH<sub>2</sub>)<sub>1-6</sub>-S-, -NR<sub>6</sub>-NR<sub>7</sub>-, -NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>7</sub>-, -NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>7</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>8</sub>-, -NR<sub>9</sub>-C(O)-, -C(O)-NR<sub>9</sub>-, -C(O)-(CH<sub>2</sub>)<sub>0-6</sub>-NR<sub>6</sub>-(CH<sub>2</sub>)<sub>0-6</sub>-C(O)-, -NR<sub>6</sub>-(CH<sub>2</sub>)<sub>0-6</sub>-C(O)-(CH<sub>2</sub>)<sub>1-6</sub>-C(O)-(CH<sub>2</sub>)<sub>0-6</sub>-NR<sub>7</sub>-, -NR<sub>6</sub>-C(O)-NR<sub>7</sub>-, -NR<sub>6</sub>-C(NR<sub>7</sub>)-NR<sub>8</sub>-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-S-, -S-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-O-, -S-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-S- and -NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-S-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>7</sub>- (wherein R<sub>6</sub>, R<sub>7</sub> and R<sub>8</sub> are independently selected from the group consisting of hydrogen, C<sub>1-8</sub>alkyl, C<sub>1-8</sub>alkoxy(C<sub>1-8</sub>)alkyl, carboxyl(C<sub>1-8</sub>)alkyl, amino(C<sub>1-8</sub>)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), hydroxy(C<sub>1-8</sub>)alkyl, heterocyclyl(C<sub>1-8</sub>)alkyl, aryl(C<sub>1-8</sub>)alkyl and heteroaryl(C<sub>1-8</sub>)alkyl (wherein the foregoing heterocyclyl, aryl and heteroaryl substituents are optionally substituted with one to four substituents independently selected from the group consisting of C<sub>1-8</sub>alkyl, C<sub>1-8</sub>alkoxy, C<sub>1-8</sub>alkoxy(C<sub>1-8</sub>)alkyl, carboxyl, carboxyl(C<sub>1-8</sub>)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), amino(C<sub>1-8</sub>)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), halogen, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkyl, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkoxy, hydroxy and hydroxy(C<sub>1-8</sub>)alkyl; and, wherein heterocyclyl is optionally substituted with oxo); and, wherein R<sub>9</sub> is selected from the group

- consisting of C<sub>1-8</sub>alkyl, C<sub>1-8</sub>alkoxy(C<sub>1-8</sub>)alkyl, carboxyl(C<sub>1-8</sub>)alkyl, amino(C<sub>1-8</sub>)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), hydroxy(C<sub>1-8</sub>)alkyl, heterocyclyl(C<sub>1-8</sub>)alkyl, aryl(C<sub>1-8</sub>)alkyl and heteroaryl(C<sub>1-8</sub>)alkyl (wherein the foregoing heterocyclyl, aryl and heteroaryl substituents are optionally substituted with one to four substituents independently selected from the group consisting of C<sub>1-8</sub>alkyl, C<sub>1-8</sub>alkoxy, C<sub>1-8</sub>alkoxy(C<sub>1-8</sub>)alkyl, carboxyl, carboxyl(C<sub>1-8</sub>)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), amino(C<sub>1-8</sub>)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), halogen, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkyl, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkoxy, hydroxy and hydroxy(C<sub>1-8</sub>)alkyl; and, wherein heterocyclyl is optionally substituted with oxo)); and,
- 15 R<sub>1</sub> and R<sub>3</sub> are independently selected from the group consisting of hydrogen, C<sub>1-8</sub>alkyl, C<sub>2-8</sub>alkenyl, C<sub>2-8</sub>alkynyl (wherein alkyl, alkenyl and alkynyl are optionally substituted with a substituent selected from the group consisting of C<sub>1-8</sub>alkoxy, alkoxy(C<sub>1-8</sub>)alkyl, carboxyl, carboxyl(C<sub>1-8</sub>)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), amino(C<sub>1-8</sub>)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), (halo)<sub>1-3</sub>, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkyl, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkoxy, hydroxy, hydroxy(C<sub>1-8</sub>)alkyl and oxo), C<sub>1-8</sub>alkoxy, C<sub>1-8</sub>alkoxycarbonyl, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkoxy, C<sub>1-8</sub>alkylthio, aryl, heteroaryl (wherein aryl and heteroaryl are optionally substituted with a substituent selected from the group consisting of C<sub>1-8</sub>alkyl, C<sub>1-8</sub>alkoxy, alkoxy(C<sub>1-8</sub>)alkyl, carboxyl, carboxyl(C<sub>1-8</sub>)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), amino(C<sub>1-8</sub>)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), halogen, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkyl, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkoxy, hydroxy and hydroxy(C<sub>1-8</sub>)alkyl), amino (substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), cyano, halogen, hydroxy and nitro;

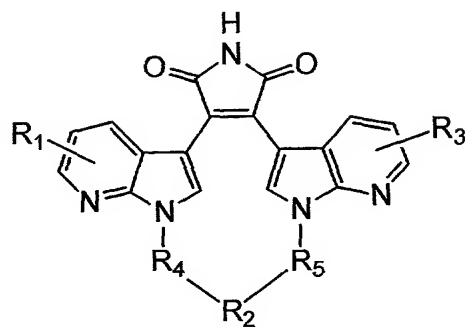


and pharmaceutically acceptable salts thereof.

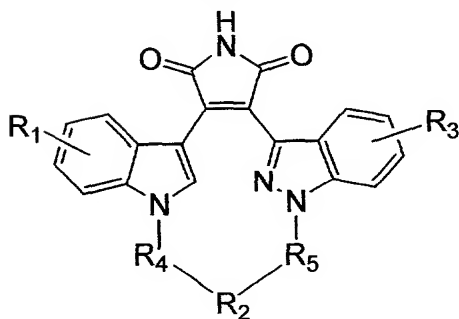
12. The compound of claim 1 wherein a compound of Formula (I) is selected from the group consisting of:



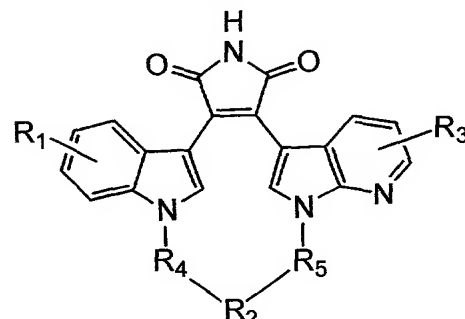
Formula (Ia);



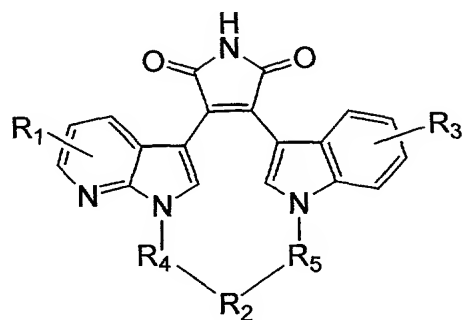
Formula (Ib);



Formula (If);



Formula (Ii); and,



Formula (Ij);

5 wherein

R<sub>4</sub> and R<sub>5</sub> are independently selected from C<sub>1-8</sub>alkyl-, C<sub>2-8</sub>alkenyl- and C<sub>2-8</sub>alkynyl- optionally substituted with oxo;

R<sub>2</sub> is selected from the group consisting of -C<sub>1-8</sub>alkyl-, -C<sub>2-8</sub>alkenyl-, -C<sub>2-8</sub>alkynyl-,  
 10 -O-(C<sub>1-8</sub>)alkyl-O-, -O-(C<sub>2-8</sub>)alkenyl-O-, -O-(C<sub>2-8</sub>)alkynyl-O-,

-C(O)-(C<sub>1-8</sub>)alkyl-C(O)- (wherein any of the foregoing alkyl, alkenyl and alkynyl linking groups are straight carbon chains optionally substituted with one to four substituents independently selected from the group consisting of C<sub>1-8</sub>alkyl, C<sub>1-8</sub>alkoxy, C<sub>1-8</sub>alkoxy(C<sub>1-8</sub>)alkyl, carboxyl, carboxyl(C<sub>1-8</sub>)alkyl, -C(O)O-(C<sub>1-8</sub>)alkyl, -C<sub>1-8</sub>alkyl-C(O)O-(C<sub>1-8</sub>)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), amino(C<sub>1-8</sub>)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), halogen, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkyl, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkoxy, hydroxy, hydroxy(C<sub>1-8</sub>)alkyl and oxo; and, wherein any of the foregoing alkyl, alkenyl and alkynyl linking groups are optionally substituted with one to two substituents independently selected from the group consisting of heterocyclyl, aryl, heteroaryl, heterocyclyl(C<sub>1-8</sub>)alkyl, aryl(C<sub>1-8</sub>)alkyl, heteroaryl(C<sub>1-8</sub>)alkyl, spirocycloalkyl and spiroheterocyclyl (wherein any of the foregoing cycloalkyl, heterocyclyl, aryl and heteroaryl substituents are optionally substituted with one to four substituents independently selected from the group consisting of C<sub>1-8</sub>alkyl, C<sub>1-8</sub>alkoxy, C<sub>1-8</sub>alkoxy(C<sub>1-8</sub>)alkyl, carboxyl, carboxyl(C<sub>1-8</sub>)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), amino(C<sub>1-8</sub>)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), halogen, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkyl, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkoxy, hydroxy and hydroxy(C<sub>1-8</sub>)alkyl; and, wherein any of the foregoing heterocyclyl substituents are optionally substituted with oxo)), cycloalkyl, heterocyclyl, aryl, heteroaryl (wherein cycloalkyl, heterocyclyl, aryl and heteroaryl are optionally substituted with one to four substituents independently selected from the group consisting of C<sub>1-8</sub>alkyl, C<sub>1-8</sub>alkoxy, C<sub>1-8</sub>alkoxy(C<sub>1-8</sub>)alkyl, carboxyl, carboxyl(C<sub>1-8</sub>)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), amino(C<sub>1-8</sub>)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), halogen, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkyl, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkoxy, hydroxy and hydroxy(C<sub>1-8</sub>)alkyl; and, wherein heterocyclyl is optionally substituted with oxo), -(O-(CH<sub>2</sub>)<sub>1-6</sub>)<sub>0.5</sub>-O-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-O-(CH<sub>2</sub>)<sub>1-6</sub>-O-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-O-(CH<sub>2</sub>)<sub>1-6</sub>-O-(CH<sub>2</sub>)<sub>1-6</sub>-O-, -(O-(CH<sub>2</sub>)<sub>1-6</sub>)<sub>0.5</sub>-NR<sub>6</sub>-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-O-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-O-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>6</sub>-, -(O-(CH<sub>2</sub>)<sub>1-6</sub>)<sub>0.5</sub>-S-,

- O-(CH<sub>2</sub>)<sub>1-6</sub>-S-(CH<sub>2</sub>)<sub>1-6</sub>-O-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-O-(CH<sub>2</sub>)<sub>1-6</sub>-S-, -NR<sub>6</sub>-, -NR<sub>6</sub>-NR<sub>7</sub>-,  
 -NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>7</sub>-, -NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>7</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>8</sub>-, -NR<sub>6</sub>-C(O)-, -C(O)-NR<sub>6</sub>-,  
 -C(O)-(CH<sub>2</sub>)<sub>0-6</sub>-NR<sub>6</sub>-(CH<sub>2</sub>)<sub>0-6</sub>-C(O)-,  
 -NR<sub>6</sub>-(CH<sub>2</sub>)<sub>0-6</sub>-C(O)-(CH<sub>2</sub>)<sub>1-6</sub>-C(O)-(CH<sub>2</sub>)<sub>0-6</sub>-NR<sub>7</sub>-, -NR<sub>6</sub>-C(O)-NR<sub>7</sub>-,  
 5 -NR<sub>6</sub>-C(NR<sub>7</sub>)-NR<sub>8</sub>-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-S-, -S-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-O-,  
 -S-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-S-, -NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-S-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>7</sub>- and -SO<sub>2</sub>- (wherein  
 R<sub>6</sub>, R<sub>7</sub> and R<sub>8</sub> are independently selected from the group consisting of hydrogen,  
 C<sub>1-8</sub>alkyl, C<sub>1-8</sub>alkoxy(C<sub>1-8</sub>)alkyl, carboxyl(C<sub>1-8</sub>)alkyl, amino(C<sub>1-8</sub>)alkyl (wherein  
 amino is substituted with a substituent independently selected from the group  
 10 consisting of hydrogen and C<sub>1-4</sub>alkyl), hydroxy(C<sub>1-8</sub>)alkyl, heterocyclyl(C<sub>1-8</sub>)alkyl,  
 aryl(C<sub>1-8</sub>)alkyl and heteroaryl(C<sub>1-8</sub>)alkyl (wherein the foregoing heterocyclyl, aryl  
 and heteroaryl substituents are optionally substituted with one to four substituents  
 independently selected from the group consisting of C<sub>1-8</sub>alkyl, C<sub>1-8</sub>alkoxy,  
 C<sub>1-8</sub>alkoxy(C<sub>1-8</sub>)alkyl, carboxyl, carboxyl(C<sub>1-8</sub>)alkyl, amino (substituted with a  
 15 substituent independently selected from the group consisting of hydrogen and  
 C<sub>1-4</sub>alkyl), amino(C<sub>1-8</sub>)alkyl (wherein amino is substituted with a substituent  
 independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl),  
 halogen, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkyl, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkoxy, hydroxy and hydroxy(C<sub>1-8</sub>)alkyl;  
 and, wherein heterocyclyl is optionally substituted with oxo));  
 20 with the proviso that, if A and E are selected from a hydrogen substituted carbon atom,  
 then R<sub>2</sub> is selected from the group consisting of -C<sub>2-8</sub>alkynyl-, -O-(C<sub>1-8</sub>)alkyl-O-,  
 -O-(C<sub>2-8</sub>)alkenyl-O-, -O-(C<sub>2-8</sub>)alkynyl-O-, -C(O)-(C<sub>1-8</sub>)alkyl-C(O)- (wherein any of  
 the foregoing alkyl, alkenyl and alkynyl linking groups are straight carbon chains  
 optionally substituted with one to four substituents independently selected from the  
 25 group consisting of C<sub>1-8</sub>alkyl, C<sub>1-8</sub>alkoxy, C<sub>1-8</sub>alkoxy(C<sub>1-8</sub>)alkyl, carboxyl,  
 carboxyl(C<sub>1-8</sub>)alkyl, -C(O)O-(C<sub>1-8</sub>)alkyl, -C<sub>1-8</sub>alkyl-C(O)O-(C<sub>1-8</sub>)alkyl, amino  
 (substituted with a substituent independently selected from the group consisting of  
 hydrogen and C<sub>1-4</sub>alkyl), amino(C<sub>1-8</sub>)alkyl (wherein amino is substituted with a  
 substituent independently selected from the group consisting of hydrogen and  
 30 C<sub>1-4</sub>alkyl), halogen, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkyl, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkoxy, hydroxy,  
 hydroxy(C<sub>1-8</sub>)alkyl and oxo; and, wherein any of the foregoing alkyl, alkenyl and  
 alkynyl linking groups are optionally substituted with one to two substituents  
 independently selected from the group consisting of heterocyclyl, aryl, heteroaryl,

heterocyclyl(C<sub>1-8</sub>)alkyl, aryl(C<sub>1-8</sub>)alkyl, heteroaryl(C<sub>1-8</sub>)alkyl, spirocycloalkyl and spiroheterocyclyl (wherein any of the foregoing cycloalkyl, heterocyclyl, aryl and heteroaryl substituents are optionally substituted with one to four substituents independently selected from the group consisting of C<sub>1-8</sub>alkyl, C<sub>1-8</sub>alkoxy, C<sub>1-8</sub>alkoxy(C<sub>1-8</sub>)alkyl, carboxyl, carboxyl(C<sub>1-8</sub>)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), amino(C<sub>1-8</sub>)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), halogen, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkyl, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkoxy, hydroxy and hydroxy(C<sub>1-8</sub>)alkyl; and, wherein any of the foregoing heterocyclyl substituents are optionally substituted with oxo)), cycloalkyl (wherein cycloalkyl is optionally substituted with one to four substituents independently selected from the group consisting of C<sub>1-8</sub>alkyl, C<sub>1-8</sub>alkoxy, C<sub>1-8</sub>alkoxy(C<sub>1-8</sub>)alkyl, carboxyl, carboxyl(C<sub>1-8</sub>)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), amino(C<sub>1-8</sub>)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), halogen, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkyl, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkoxy, hydroxy and hydroxy(C<sub>1-8</sub>)alkyl), -(O-(CH<sub>2</sub>)<sub>1-6</sub>)<sub>1-5</sub>-O-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-O-(CH<sub>2</sub>)<sub>1-6</sub>-O-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-O-(CH<sub>2</sub>)<sub>1-6</sub>-O-(CH<sub>2</sub>)<sub>1-6</sub>-O-, -(O-(CH<sub>2</sub>)<sub>1-6</sub>)<sub>1-5</sub>-NR<sub>6</sub>-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-O-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-O-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>6</sub>-, -(O-(CH<sub>2</sub>)<sub>1-6</sub>)<sub>0-5</sub>-S-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-S-(CH<sub>2</sub>)<sub>1-6</sub>-O-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-O-(CH<sub>2</sub>)<sub>1-6</sub>-S-, -NR<sub>6</sub>-NR<sub>7</sub>-, -NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>7</sub>-, -NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>7</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>8</sub>-, -NR<sub>9</sub>-C(O)-, -C(O)-NR<sub>9</sub>-, -C(O)-(CH<sub>2</sub>)<sub>0-6</sub>-NR<sub>6</sub>-(CH<sub>2</sub>)<sub>0-6</sub>-C(O)-, -NR<sub>6</sub>-(CH<sub>2</sub>)<sub>0-6</sub>-C(O)-(CH<sub>2</sub>)<sub>1-6</sub>-C(O)-(CH<sub>2</sub>)<sub>0-6</sub>-NR<sub>7</sub>-, -NR<sub>6</sub>-C(O)-NR<sub>7</sub>-, -NR<sub>6</sub>-C(NR<sub>7</sub>)-NR<sub>8</sub>-, -O-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-S-, -S-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-O-, -S-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-S- and -NR<sub>6</sub>-(CH<sub>2</sub>)<sub>1-6</sub>-S-(CH<sub>2</sub>)<sub>1-6</sub>-NR<sub>7</sub>- (wherein R<sub>6</sub>, R<sub>7</sub> and R<sub>8</sub> are independently selected from the group consisting of hydrogen, C<sub>1-8</sub>alkyl, C<sub>1-8</sub>alkoxy(C<sub>1-8</sub>)alkyl, carboxyl(C<sub>1-8</sub>)alkyl, amino(C<sub>1-8</sub>)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), hydroxy(C<sub>1-8</sub>)alkyl, heterocyclyl(C<sub>1-8</sub>)alkyl, aryl(C<sub>1-8</sub>)alkyl and heteroaryl(C<sub>1-8</sub>)alkyl (wherein the foregoing heterocyclyl, aryl and heteroaryl substituents are optionally substituted with one to four substituents independently selected from the group consisting of C<sub>1-8</sub>alkyl, C<sub>1-8</sub>alkoxy, C<sub>1-8</sub>alkoxy(C<sub>1-8</sub>)alkyl,

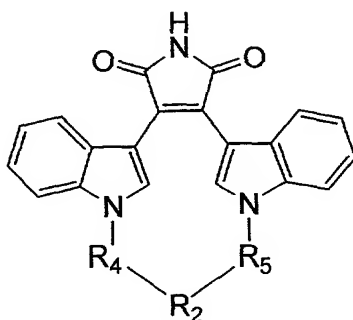
carboxyl, carboxyl(C<sub>1-8</sub>)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), amino(C<sub>1-8</sub>)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), halogen, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkyl, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkoxy, hydroxy and hydroxy(C<sub>1-8</sub>)alkyl; and, wherein heterocyclyl is optionally substituted with oxo); and, wherein R<sub>9</sub> is selected from the group consisting of C<sub>1-8</sub>alkyl, C<sub>1-8</sub>alkoxy(C<sub>1-8</sub>)alkyl, carboxyl(C<sub>1-8</sub>)alkyl, amino(C<sub>1-8</sub>)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), hydroxy(C<sub>1-8</sub>)alkyl, heterocyclyl(C<sub>1-8</sub>)alkyl, aryl(C<sub>1-8</sub>)alkyl and heteroaryl(C<sub>1-8</sub>)alkyl (wherein the foregoing heterocyclyl, aryl and heteroaryl substituents are optionally substituted with one to four substituents independently selected from the group consisting of C<sub>1-8</sub>alkyl, C<sub>1-8</sub>alkoxy, C<sub>1-8</sub>alkoxy(C<sub>1-8</sub>)alkyl, carboxyl, carboxyl(C<sub>1-8</sub>)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), amino(C<sub>1-8</sub>)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), halogen, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkyl, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkoxy, hydroxy and hydroxy(C<sub>1-8</sub>)alkyl; and, wherein heterocyclyl is optionally substituted with oxo)); and,

R<sub>1</sub> and R<sub>3</sub> are independently selected from the group consisting of hydrogen, C<sub>1-8</sub>alkyl, C<sub>2-8</sub>alkenyl, C<sub>2-8</sub>alkynyl (wherein alkyl, alkenyl and alkynyl are optionally substituted with a substituent selected from the group consisting of C<sub>1-8</sub>alkoxy, alkoxy(C<sub>1-8</sub>)alkyl, carboxyl, carboxyl(C<sub>1-8</sub>)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), amino(C<sub>1-8</sub>)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), (halo)<sub>1-3</sub>, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkyl, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkoxy, hydroxy, hydroxy(C<sub>1-8</sub>)alkyl and oxo), C<sub>1-8</sub>alkoxy, C<sub>1-8</sub>alkoxycarbonyl, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkoxy, C<sub>1-8</sub>alkylthio, aryl, heteroaryl (wherein aryl and heteroaryl are optionally substituted with a substituent selected from the group consisting of C<sub>1-8</sub>alkyl, C<sub>1-8</sub>alkoxy, alkoxy(C<sub>1-8</sub>)alkyl, carboxyl, carboxyl(C<sub>1-8</sub>)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), amino(C<sub>1-8</sub>)alkyl

- (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), halogen, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkyl, (halo)<sub>1-3</sub>(C<sub>1-8</sub>)alkoxy, hydroxy and hydroxy(C<sub>1-8</sub>)alkyl), amino (substituted with a substituent independently selected from the group consisting of hydrogen and C<sub>1-4</sub>alkyl), cyano, halogen, hydroxy and nitro;

and pharmaceutically acceptable salts thereof.

13. A compound of Formula (Ia1):

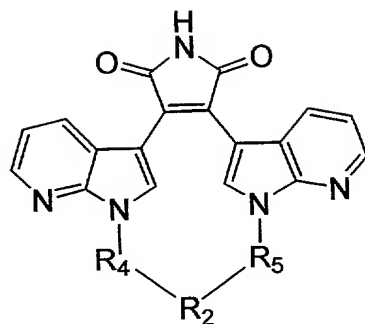


Formula (Ia1)

- 10 wherein R<sub>4</sub>, R<sub>2</sub> and R<sub>5</sub> are dependently selected from:

R <sub>4</sub>	R <sub>2</sub>	R <sub>5</sub>
-(CH <sub>2</sub> ) <sub>2</sub> -	-O-(CH <sub>2</sub> ) <sub>2</sub> -O-	-(CH <sub>2</sub> ) <sub>2</sub> -;
-(CH <sub>2</sub> ) <sub>2</sub> -	-O-(CH <sub>2</sub> ) <sub>2</sub> -O-(CH <sub>2</sub> ) <sub>2</sub> -O-	-(CH <sub>2</sub> ) <sub>2</sub> -;
-(CH <sub>2</sub> ) <sub>2</sub> -	-O-(CH <sub>2</sub> ) <sub>2</sub> -O-(CH <sub>2</sub> ) <sub>2</sub> -O-(CH <sub>2</sub> ) <sub>2</sub> -O-	-(CH <sub>2</sub> ) <sub>2</sub> -;
-(CH <sub>2</sub> ) <sub>2</sub> -	-O-(CH <sub>2</sub> ) <sub>2</sub> -O-(CH <sub>2</sub> ) <sub>2</sub> -O-(CH <sub>2</sub> ) <sub>2</sub> -O-	-(CH <sub>2</sub> ) <sub>2</sub> -;
-(CH <sub>2</sub> ) <sub>2</sub> -	-O-(CH <sub>2</sub> ) <sub>2</sub> -N(Et)-(CH <sub>2</sub> ) <sub>2</sub> -O-	-(CH <sub>2</sub> ) <sub>2</sub> -;
-(CH <sub>2</sub> ) <sub>2</sub> -	-O-(CH <sub>2</sub> ) <sub>2</sub> -N(Me)-(CH <sub>2</sub> ) <sub>2</sub> -O-	-(CH <sub>2</sub> ) <sub>2</sub> -;
-(CH <sub>2</sub> ) <sub>2</sub> -	-O-(CH <sub>2</sub> ) <sub>2</sub> -N( <i>i</i> -Pr)-(CH <sub>2</sub> ) <sub>2</sub> -O-	-(CH <sub>2</sub> ) <sub>2</sub> -;
-(CH <sub>2</sub> ) <sub>2</sub> -	-N(Me)-(CH <sub>2</sub> ) <sub>2</sub> -N(Me)-(CH <sub>2</sub> ) <sub>2</sub> -N(Me)-	-(CH <sub>2</sub> ) <sub>2</sub> -;
-(CH <sub>2</sub> ) <sub>2</sub> -	-O-(CH <sub>2</sub> ) <sub>2</sub> -N(2-hydroxy-Et)-(CH <sub>2</sub> ) <sub>2</sub> -O-	-(CH <sub>2</sub> ) <sub>2</sub> -;
and,		
-(CH <sub>2</sub> ) <sub>2</sub> -	-O-(CH <sub>2</sub> ) <sub>2</sub> -O-(CH <sub>2</sub> ) <sub>2</sub> -N(Me)-	-(CH <sub>2</sub> ) <sub>3</sub> -.

14. A compound of Formula (Ib1):

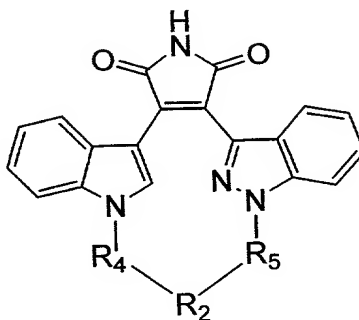


Formula (Ib1)

wherein  $R_4$ ,  $R_2$  and  $R_5$  are dependently selected from:

$R_4$	$R_2$	$R_5$
$-(CH_2)_2-$	$-O-(CH_2)_2-O-(CH_2)_2-O-$	$-(CH_2)_2-$
$-(CH_2)_2-$	$-O-(CH_2)_2-O-(CH_2)_2-O-(CH_2)_2-O-$	$-(CH_2)_2-$
$-(CH_2)_2-$	$-O-(CH_2)_2-O-(CH_2)_2-O-(CH_2)_2-O-(CH_2)_2-O-$	$-(CH_2)_2-$
$-(CH_2)_2-$	$-O-(CH_2)_2-N(Et)-(CH_2)_2-O-$	$-(CH_2)_2-$
$-(CH_2)_2-$	$-O-(CH_2)_2-S-(CH_2)_2-O-$	$-(CH_2)_2-$
$-(CH_2)_5-$	$-NH-$	$-(CH_2)_5-$
$-(CH_2)_5-$	$-N(Et)-$	$-(CH_2)_5-$
$-(CH_2)_5-$	$-NH-$	$-(CH_2)_4-$
$-(CH_2)_5-$	$-N(Et)-$	$-(CH_2)_4-$
$-(CH_2)_4-$	$-2,6\text{-pyridinyl-}$	$-(CH_2)_4-$
$-(CH_2)_4-$	$-C(O)-(CH_2)_2-$	$-(CH_2)_4-$
$-(CH_2)_4-$	$-C(O)-$	$-(CH_2)_4-$
$-CH_2-$	$-CH[R](OH)-(CH_2)_6-CH[R](OH)-$	$-CH_2-$
and,		
$-(CH_2)_2-$	$-O-(CH_2)_2-O-$	$-(CH_2)_2-$

15. A compound of Formula (If1):

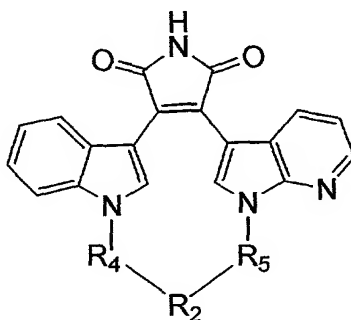


## Formula (If1)

wherein  $R_4$ ,  $R_2$  and  $R_5$  are dependently selected from:

$R_4$	$R_2$	$R_5$
$-(CH_2)_2-$	$-O-(CH_2)_2-N(Me)-(CH_2)_2-O-$	$-(CH_2)_2-$ ;
$-(CH_2)_2-$	$-O-(CH_2)_2-N(Et)-(CH_2)_2-O-$	$-(CH_2)_2-$ ;
and,		
$-(CH_2)_2-$	$-O-(CH_2)_2-N(2-OMe-Et)-(CH_2)_2-O-$	$-(CH_2)_2-$ .

16. A compound of Formula (Ii1):



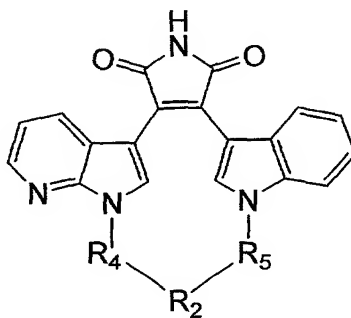
Formula (Ii1)

wherein  $R_4$ ,  $R_2$  and  $R_5$  are dependently selected from:

$R_4$	$R_2$	$R_5$
$-CH_2-$	-1,3-phenyl-	$-CH_2-$ ;
and,		
$-CH_2-$	-2,6-pyridinyl-	$-CH_2-$ .

5

17. A compound of Formula (Ij1):

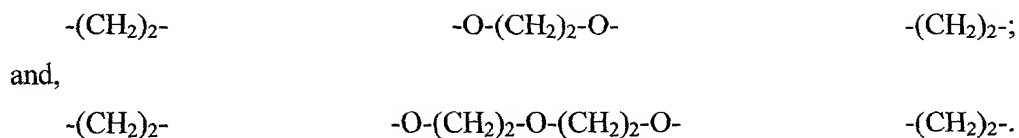


Formula (Ij1)

wherein  $R_4$ ,  $R_2$  and  $R_5$  are dependently selected from:

$R_4$	$R_2$	$R_5$
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18. A pharmaceutical composition comprising a compound of claim 1 and a pharmaceutically acceptable carrier.
- 5 19. A pharmaceutical composition made by mixing a compound of claim 1 and a pharmaceutically acceptable carrier.
20. A method for preparing a pharmaceutical composition comprising mixing a compound of claim 1 and a pharmaceutically acceptable carrier.
- 10 21. A method for treating or ameliorating a kinase mediated disorder comprising administering to a subject in need thereof a therapeutically effective amount of a compound of claim 1.
- 15 22. The method of claim 21 wherein the disorder is mediated by selective inhibition of a kinase selected from the group consisting of protein kinase C and glycogen synthase kinase-3.
- 20 23. The method of claim 22 wherein the kinase is selected from the group consisting of protein kinase C  $\alpha$ , protein kinase C  $\beta$ -II, protein kinase C  $\gamma$  and glycogen synthase kinase-3 $\beta$ .
- 25 24. The method of claim 21 wherein the disorder is mediated by dual inhibition of at least two kinases selected from the group consisting of protein kinase C and glycogen synthase kinase-3.
- 30 25. The method of claim 24 wherein at least two kinases are selected from the group consisting of protein kinase C  $\alpha$ , protein kinase C  $\beta$ -II, protein kinase C  $\gamma$  and glycogen synthase kinase-3 $\beta$ .

26. The method of claim 21 wherein the therapeutically effective amount of the compound of claim 1 is from about 0.001 mg/kg/day to about 300 mg/kg/day.
27. The method of claim 21 wherein the kinase mediated disorder is selected from the group consisting of cardiovascular diseases, diabetes, diabetes-associated disorders, inflammatory diseases, immunological disorders, dermatological disorders, oncological disorders and CNS disorders.
28. The method of claim 27 wherein cardiovascular diseases are selected from the group consisting of acute stroke, heart failure, cardiovascular ischemia, thrombosis, atherosclerosis, hypertension, restenosis, retinopathy of prematurity and age-related macular degeneration.
29. The method of claim 27 wherein diabetes is selected from the group consisting of insulin dependent diabetes and Type II non-insulin dependent diabetes mellitus.
30. The method of claim 27 wherein diabetes-associated disorders are selected from the group consisting of impaired glucose tolerance, diabetic retinopathy, proliferative retinopathy, retinal vein occlusion, macular edema, cardiomyopathy, nephropathy and neuropathy.
31. The method of claim 27 wherein inflammatory diseases are selected from the group consisting of vascular permeability, inflammation, asthma, rheumatoid arthritis and osteoarthritis.
32. The method of claim 27 wherein immunological disorders are selected from the group consisting of transplant tissue rejection, HIV-1 and PKC modulated immunological disorders.
33. The method of claim 27 wherein dermatological disorders are selected from the group consisting of psoriasis, hair loss and baldness.

34. The method of claim 27 wherein oncological disorders are selected from the group consisting of cancer, tumor growth, uncontrolled cell proliferation, proliferative angiopathy and angiogenesis.
- 5 35. The method of claim 27 wherein central nervous system disorders are selected from the group consisting of chronic pain, neuropathic pain, epilepsy, chronic neurodegenerative conditions, dementia, Alzheimer's disease, mood disorders, schizophrenia, manic depression and neurotraumatic, cognitive decline and ischemia-related diseases.
- 10 36. The method of claim 21 further comprising a method for use for a compound of claim 1 as an adjunct to chemotherapy and radiation therapy.
- 15 37. The method of claim 21 further comprising administering to a subject in need thereof a therapeutically effective amount of a pharmaceutical composition of claim 18.
- 20 38. The method of claim 37 wherein the therapeutically effective amount of a pharmaceutical composition of claim 18 is from about 0.001 mg/kg/day to about 300 mg/kg/day.
- 25 39. The method of claim 35 wherein ischemia-related diseases are those resulting from head trauma or transient ischemic stroke.